ORGANIC
LETTERS

2008
Vol. 10, No. 11
2303−2305

Highly Sterically Hindered Olefins: A Case of *E*- and *Z*-Di-*tert*-butyl α,*β*-Unsaturated Acids

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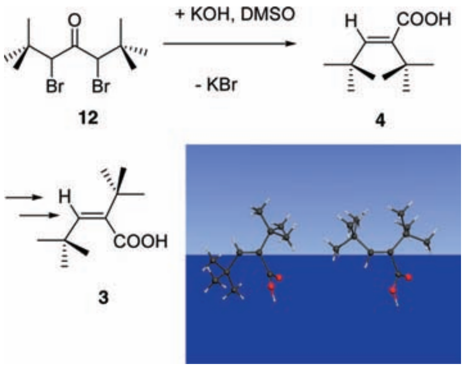
Received April 10, 2008

ABSTRACT



Use of a superbase in the Favorskii rearrangement of 12 resulted in the synthesis of highly sterically hindered olefins, (*E*)-2-*tert*-butyl-4,4-dimethyl-pent-2-enoic acid (4) and (*Z*)-2-*tert*-butyl-4,4-dimethyl-pent-2-enoic acid (3).

Sterically hindered tetra-*tert*-butylethylene **1** is a deceptively simple molecule, with no "exotic" functionality and is predicted to be stable. Yet it has eluded synthesis for over 50 years.[1] Chemists are interested in this molecule because its highly strained nature should affect several structural parameters. Also, steric hindrance can kinetically stabilize unusual classes of compounds such as **1** and its analogues, making them interesting targets for use as synthetic building blocks. The functionalization of **1** by carboxyl groups has been attempted without success. Similarly, the α,*β*-unsaturated carboxyl acid with three *tert*-butyl groups (**2**) is unknown (Scheme 1).[2] On the other hand, monosubstituted *tert*-butyl α,*β*-unsaturated carboxyl acids **6**, **7**, and **8** have been prepared by a variety of methodologies including Claisen−Schmidt condensation, Peterson olefination, Ni- and Pd-catalyzed hydroxycarbonylation of terminal alkynes, olefin cross metathesis, carbonylation of vinylmercurial derivatives, and Favorskii rearrangement.[3]

The extension of the Favorskii methodology to the synthesis of disubstituted *tert*-butyl α,*β*-unsaturated carboxyl

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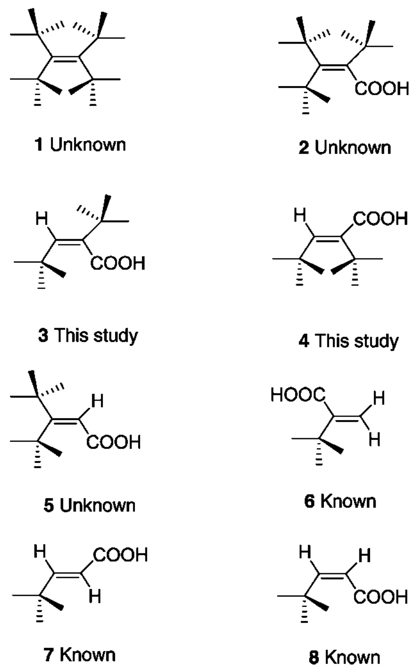
10.1021/ol800808g CCC: $40.75

Scheme 1



acids **3** and **4** failed to produce the desired acids.[2] Instead, the Favorskii approach led to the isolation of di-*tert*-butylcyclopropenone and substituted di-*tert*-butylcyclopropenyl cations, which can be considered as potential intermediates to disubstituted *tert*-butyl α,β-unsaturated carboxyl acids **3** and **4**.[4] In this study we report the application of a superbase in the Favorskii rearrangement, which let us overcome previous difficulties in the synthesis of **3** and **4**.

Dineopentyl ketone (**11**) was synthesized by the reaction of neopentylmagnesium chloride with *tert*-butylacetic acid chloride in THF at −78 °C with 58% yield after distillation (Scheme 2). The dibromination of **11** was carried out in glacial acetic acid, an environmentally friendlier alternative to bromination in chloroform.[4a] The Favorskii rearrangement of **12** was carried out in DMSO with a slight excess of KOH. The inexpensive mixture of KOH in DMSO is widely known as a superbase for facilitating difficult organic transformation.[5] After base/acid extractions (see Supporting Information), the (*E*)-2-*tert*-butyl-4,4-dimethyl-pent-2-enoic acid (**4**) was isolated as colorless crystals with mp 79.09 °C. Monitoring the progress of the Favorskii rearrangement by ^{1}H and ^{13}C NMR spectrometry confirms that only one isomer was formed at this step. Thus, the ^{1}H NMR spectrum of **4** consists of two singlets at 1.10 and 1.30 ppm for two *tert*-butyl groups, one singlet at 6.30 ppm for a vinyl proton, and a broad signal of the acidic proton at 12.50 ppm. ^{13}C NMR spectrum of **4** has four singlets corresponding to the tertiary and primary carbons of the *tert*-butyl groups at 31.41, 31.97, 32.95, and 33.83 ppm and three singlets for the α,β-unsaturated moiety at 142.86, 145.01, and 179.29 ppm.

X-ray analysis (Figure 1) of **4** confirmed that it is an *E*-isomer.

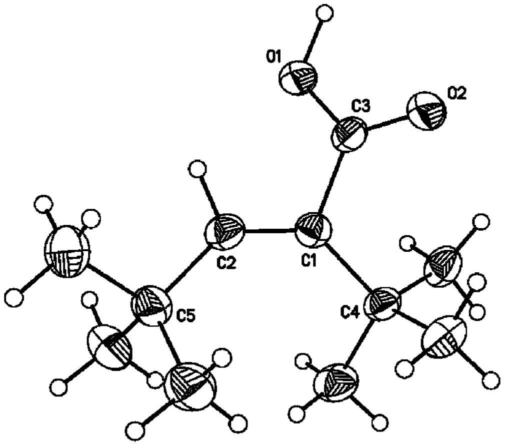
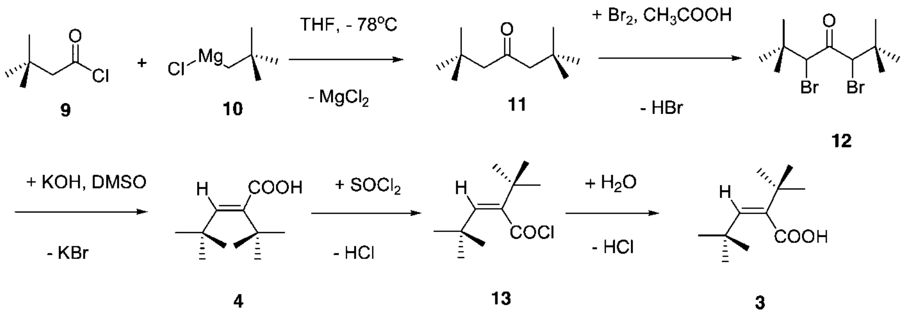


Figure 1. ORTEP drawing of (*E*)-2-*tert*-butyl-4,4-dimethyl-pent-2-enoic acid **4**. Thermal ellipsoids are drawn to the 50% probability level. Torsion angles: C5−C2−C1−C3 = −168.7(2)°; C5−C2−C1−C4 = 5.3(4)°.

The >C=C< double bond length in **4** is 1.346 Å, which is longer than the >C=C< double bond length in ethylene of 1.313 Å.[6a] However, it is close to the bond lengths of known sterically hindered tetra-substituted olefins (1.349−1.358 Å),[1e] and is even closer to a calculated value of 1.342 Å for tri-*tert*-butylethylene.[6b] The close proximity of two *cis*-*tert*-butyl groups in **4** causes the >C=C< double bond to twist and deviate from planarity to −168.7(2)° in the C5−C2−C1−C3 sequence. This experimental value is

Scheme 2



situated just between two torsion angles of −162.2° and − 174.3° calculated for tri-*tert*-butylethylene.[6b]

The Favorskii rearrangement is known to produce α,*β*-unsaturated carboxyl acids in a geometrically selective manner. In this instance, the hydroxyl anion attacks the carbonyl group of intermediate di-*tert*-butylcyclopropenone from the opposite side of di-*tert*-butyl substituents, affording *E*-geometry of the $>$C=C$<$ bond.[7]

Isomerization from *E*-geometry to *Z*-geometry was observed when acid **4** was transformed to the acid chloride **13** with the possibility of HCl acting as a catalyst for this isomerization (Scheme 2). According to ^{1}H and ^{13}C NMR spectra of **13**, it was prepared as a single isomer. The ^{1}H NMR spectrum of **13** consists of two singlets for the *tert*-butyl groups at 1.10 and 1.20 ppm and one singlet at 5.40 ppm for a vinyl proton. The ^{13}C NMR spectrum of **4** reveals two singlets corresponding to tertiary carbons at 34.12 and 35.84 ppm and two singlets for the primary carbons of *tert*-butyl groups at 29.04 and 30.89 ppm. The expected three singlets for the α,*β*-unsaturated moiety were observed at 137.18, 144.67, and 171.41 ppm.

A sample of **13**, which is a liquid, was hydrolyzed, and a crystal was grown to establish the geometry around the $>$C=C$<$ double bond. According to X-ray analysis, **3** is a *Z*-isomer (Figure 2).

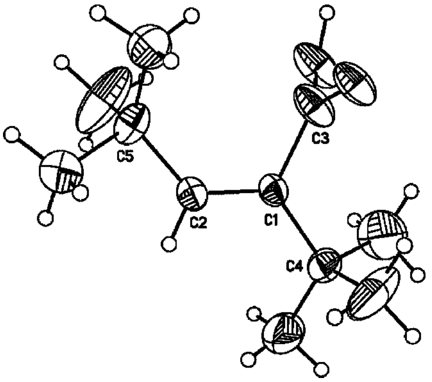


Figure 2. ORTEP drawing of (*Z*)-2-*tert*-butyl-4,4-dimethyl-pent-2-enoic acid **3**. Thermal ellipsoids are drawn to the 30% probability level. Torsion angles: C5−C2−C1−C3 = 0.3(7)°, C5−C2−C1−C4 = 176.6(4)°.

The $>$C=C$<$ double bond length in **3** is 1.339(8) Å, similar to that in **4**. Superimposition of the two structures is shown in Figure 3, confirming that the $>$C=C$<$ double bonds and the allylic bonds are essentially identical in the *E*- and *Z*-structures. The difference is in the torsion angles. Deviation from planarity is minimal in **3**, with the biggest torsion angle in the sequence C5−C2−C1−C4 with 176.6(4)°. The decreased sterical hindrance in **3** is likely the driving force for the observed *E*/*Z*-isomerization. *E*/*Z* isomerization of monosubstituted *tert*-butyl α,*β*-unsaturated carboxyl derivatives is well-documented.[8]

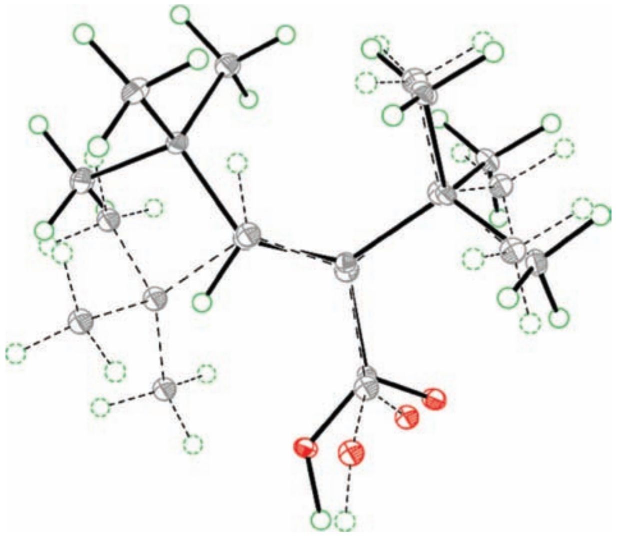


Figure 3. Superimpose picture of (*E*)- and (*Z*)-acids **4** and **3**.

In conclusion, we have developed a reliable synthetic procedure for preparing derivatives of one of the most sterically hindered olefins. The application of **13** for the stabilization of low-coordinated species of sp-elements and, particularly, phosphorus derivatives[9] will be presented in due time.[10]

Acknowledgment. Authors wish to thank Steve F. Krakowski, Randall A. Parisi, John Nguyen, and Steve A. Hill for the multinuclear NMR experiments; Vicki North for DSC measurements; and Karin Karel for proofreading the manuscript.

Supporting Information Available: Experimental preparations for **11**, **12**, **4**, **13** and **3** and crystallographic files in CIF format for **3** and **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) This is DuPont publication no. 8863.